

FORM PTO-1449 INFORMATION DISCLOSURE STATEMENT	ATTY. DOCKET NO. 0609.4270001	APPLICATION NO. 09/065,902 JUL 29 1998
	APPLICANT TANZI and KIM GROUP 1800	
	FILING DATE April 24, 1998	GROUP 1643/644

U.S. PATENT DOCUMENTS							
EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
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	AL						Yes No
	AM						Yes No
	AN						Yes No
	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
KC	AR	1	Borchelt, D.R., et al., "Familial Alzheimer's Disease-Linked Presenilin 1 Variants Elevate Aβ1-42/1-40 Ratio In Vitro and In Vivo," <i>Neuron</i> 17:1005-1013 (November 1996)
KC	AS	1	Bush, A.I., et al., "An Abnormality of Plasma Amyloid Protein Precursor in Alzheimer's Disease," <i>Annals of Neurology</i> 32:57-65 (1992)
KC	AT	1	Chinnaiyan, A.M., and Dixit, V.M., "The cell-death machine," <i>Current Biology</i> 6:555-562 (May 1996)

EXAMINER <i>Karen Clemens</i>	DATE CONSIDERED <i>3/20/00</i>
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	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
KC	AR	2	Ciechanover, A., "The Ubiquitin-Proteasome Proteolytic Pathway," <i>Cell</i> 79:13-21 (1994)
KC	AS	2	Citron, M., et al., "Mutant presenilins of Alzheimer's disease increase production of 42-residue amyloid β -protein in both transfected cells and transgenic mice," <i>Nature Medicine</i> 3:67-72 (January 1997)
KC	AT	2	Cook, D.G., et al., "Expression and analysis of presenilin 1 in a human neuronal system: Localization in cell bodies and dendrites," <i>Proc. Natl. Acad. Sci. USA</i> 93:9223-9228 (August 1996)

EXAMINER <i>Karen Clemens</i>	DATE CONSIDERED 3-20-00
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KC	AR	3	Cotman, C.W., and Anderson, A.J., "A Potential Role for Apoptosis in Neurodegeneration and Alzheimer's Disease," <i>Molecular Neurobiology</i> 10:19-45 (1995)
KC	AS	3	Deng, G., et al., "Alzheimer-associated presenilin-2 confers increased sensitivity to apoptosis in PC12 cells," <i>FEBS Letters</i> 397:50-54 (November 1996)
KC	AT	3	Doan, A., et al., "Protein Topology of Presenilin 1," <i>Neuron</i> 17:1023-1030 (November 1996)

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0609.4270001APPLICATION NO.
09/065,902

JUL 29 1998

APPLICANT
TANZI and KIM

GROUP 1800

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KC	AR	4	Duff, K., et al., "Increased amyloid- β 42(43) in brains of mice expressing mutant presenilin 1," <i>Nature</i> 383:710-713 (October 1996)
KC	AS	4	Fenteany, G., et al., "Inhibition of Proteasome Activities and Subunit-Specific Amino-Terminal Threonine Modification by Lactacystin," <i>Science</i> 268:726-731 (1995)
KC	AT	4	Finley, D., and Chau, V., "Ubiquitination," <i>Annu. Rev. Cell Biol.</i> 7:25-69 (1991)

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KC	AR	5	Forloni, G., et al., "Apoptosis mediated neurotoxicity induced by chronic application of β amyloid fragment 25-35," <i>NeuroReport</i> 4:523-526 (1993)
KC	AS	5	Guo, Q., et al., "Alzheimer's PS-1 mutation perturbs calcium homeostasis and sensitizes PC12 cells to death induced by amyloid β -peptide," <i>NeuroReport</i> 8:379-383 (December 1996)
KC	AT	5	Goldberg, Y.P., et al., "Cleavage of huntingtin by apopain, a proapoptotic cysteine protease, is modulated by the polyglutamine tract," <i>Nature Genetics</i> 13:442-449 (August 1996)

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<i>KC</i>	AR	<u>6</u>	Gossen, M., and Bujard, H., "Tight control of gene expression in mammalian cells by tetracycline-responsive promoters," <i>Proc. Natl. Acad. Sci. USA</i> 89:5547-5551 (1992)
<i>KC</i>	AS	<u>6</u>	Hochstrasser, M., "Ubiquitin, proteasomes, and the regulation of intracellular protein degradation," <i>Curr. Opin. Cell Biol.</i> 7:215-223 (1995)
<i>KC</i>	AT	<u>6</u>	Hochstrasser, M., "Protein Degradation or Regulation: Ub the Judge," <i>Cell</i> 84:813-815 (March 1996)

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<i>KC</i>	AR	Z	Inoue, S., et al., "Inhibition of Degradation of 3-Hydroxy-3-methylglutaryl-coenzyme A Reductase in Vivo by Cysteine Protease Inhibitors," <i>J. Biol. Chem.</i> 266:13311-13317 (1991)
<i>KC</i>	AS	Z	Jacobson, M.D., et al., "Programmed Cell Death in Animal Development," <i>Cell</i> 88:347-354 (February 1997)
<i>KC</i>	AT	Z	Jensen, T.J., et al., "Multiple Proteolytic Systems, Including the Proteasome, Contribute to CFTR Processing," <i>Cell</i> 83:129-135 (1995)

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KC	AR	8	Johnson, E.M., Jr., "Possible Role of Neuronal Apoptosis in Alzheimer's Disease," <i>Neurobiology of Aging</i> 15 (Suppl. 2):S187-S189 (1994)
KC	AS	8	Kim, T.-W., et al., "Proteolytic Processing and Ubiquitin-Dependent Degradation of Alzheimer-Associated Presenilin 1 and 2," <i>Soc. Neurosci. Abstr.</i> 22:727, Abstract No. 293.5 (November 1996)
KC	AT	8	Kim, T.-W., et al., "Endoproteolytic Cleavage and Proteasomal Degradation of Presenilin 2 in Transfected Cells," <i>J. Biol. Chem.</i> 272:11006-11010 (April 1997)

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	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
KC	AR	2	Kim, T.-W., et al., "Alternative Cleavage of Alzheimer-Associated Presenilins During Apoptosis by a Caspase-3 Family Protease," <i>Science</i> 277:373-376 (July 1997)
KC	AS	2	Koo, E.H., and Squazzo, S.L., "Evidence That Production and Release of Amyloid β -Protein Involves the Endocytic Pathway," <i>J. Biol. Chem.</i> 269:17386-17389 (1994)
KC	AT	2	Kovacs, D.M., et al., "Alzheimer-associated presenilins 1 and 2: Neuronal expression in brain and localization to intracellular membranes in mammalian cells," <i>Nature Medicine</i> 2:224-229 (February 1996)

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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
<i>KC</i>	AR	<u>10</u>	L'Hernault, S.W., and Arduengo, P.M., "Mutation of a Putative Sperm Membrane Protein in <i>Caenorhabditis elegans</i> Prevents Sperm Differentiation but Not Its Associated Meiotic Divisions," <i>J. Cell Biol.</i> 119:55-68 (1992)
<i>KC</i>	AS	<u>10</u>	LaFerla, F.M., et al., "The Alzheimer's A β peptide induces neurodegeneration and apoptotic cell death in transgenic mice," <i>Nature Genetics</i> 9:21-30 (1995)
<i>KC</i>	AT	<u>10</u>	LeBlanc, A., "Apoptosis and Alzheimer's Disease," in <i>Molecular Mechanisms of Dementia</i> , Wasco, W., and Tanzi, R.E., eds., Humana Press, Totowa, NJ, pp. 57-71 (November 1996)

EXAMINER <i>Karen Clemen</i>	DATE CONSIDERED <i>3/25/00</i>
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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

KC	AR	11	Lee, M.K., et al., "Expression of Presenilin 1 and 2 (PS1 and PS2) in Human and Murine Tissues," <i>J. Neurosci.</i> 16:7513-7525 (December 1996)
KC	AS	11	Levitan, D., and Greenwald, I., "Facilitation of <i>lin-12</i> -mediated signalling by <i>sel-12</i> , a <i>Caenorhabditis elegans</i> <i>S182</i> Alzheimer's disease gene," <i>Nature</i> 377:351-354 (1995)
KC	AT	11	Levy-Lahad, E., et al., "Candidate Gene for the Chromosome 1 Familial Alzheimer's Disease Locus," <i>Science</i> 269:973-977 (1995)

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KC	AR	12	Li, X., and Greenwald, I., "Membrane Topology of the C. elegans SEL-12 Presenilin," <i>Neuron</i> 17:1015-1021 (November 1996)
KC	AS	12	Martin, S.J., and Green, D.R., "Protease Activation during Apoptosis: Death by a Thousand Cuts?," <i>Cell</i> 82:349-352 (1995)
KC	AT	12	McGee, T.P., et al., "Degradation of 3-Hydroxy-3-methylglutaryl-CoA Reductase in Endoplasmic Reticulum Membranes is Accelerated as a Result of Increased Susceptibility to Proteolysis," <i>J. Biol. Chem.</i> 271:25630-25638 (October 1996)

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KC	AR	13	Page, K., et al., "In situ hybridization analysis of presenilin 1 mRNA in Alzheimer disease and in lesioned rat brain," <i>Proc. Natl. Acad. Sci. USA</i> 93:14020-14024 (November 1996)
KC	AS	13	Pai, J.-T., et al., "Purification and cDNA cloning of a second apoptosis-related cysteine protease that cleaves and activates sterol regulatory element binding proteins," <i>Proc. Natl. Acad. Sci. USA</i> 93:5437-5442 (May 1996)
KC	AT	13	Paradis, E., et al., "Amyloid β Peptide of Alzheimer's Disease Downregulates Bcl-2 and Upregulates Bax Expression in Human Neurons," <i>J. Neurosci.</i> 16:7533-7539 (December 1996)

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<i>KC</i>	AR	<u>14</u>	Perez-Tur, J., <i>et al.</i> , "A mutation in Alzheimer's disease destroying a splice acceptor site in the presenilin-1 gene," <i>NeuroReport</i> 7:297-301 (1995)
<i>KC</i>	AS	<u>14</u>	Rock, K.L., <i>et al.</i> , "Inhibitors of the Proteasome Block the Degradation of Most Cell Proteins and the Generation of Peptides Presented on MHC Class I Molecules," <i>Cell</i> 78:761-771 (1994)
<i>KC</i>	AT	<u>14</u>	Rogaev, E.I., <i>et al.</i> , "Familial Alzheimer's disease in kindreds with missense mutations in a gene on chromosome 1 related to the Alzheimer's disease type 3 gene," <i>Nature</i> 376:775-778 (1995)

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KC	AR	15	Roitelman, J., et al., "Immunological Evidence for Eight Spans in the Membrane Domain of 3-Hydroxy-3-Methylglutaryl Coenzyme A Reductase: Implications for Enzyme Degradation in the Endoplasmic Reticulum," <i>J. Cell Biol.</i> 117:959-973 (1992)
KC	AS	15	Sakai, J., et al., "Sterol-Regulated Release of SREBP-2 from Cell Membranes Requires Two Sequential Cleavages, One Within a Transmembrane Segment," <i>Cell</i> 85:1037-1046 (June 1996)
KC	AT	15	Schellenberg, G.D., "Genetic dissection of Alzheimer disease, a heterogeneous disorder," <i>Proc. Natl. Acad. Sci. USA</i> 92:8552-8559 (1995)

EXAMINER	<i>Karen Clemens</i>	DATE CONSIDERED	3/20/00
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	APPLICANT TANZI and KIM	
	FILING DATE April 24, 1998	GROUP 1643 / 44

U.S. PATENT DOCUMENTS							
EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
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FOREIGN PATENT DOCUMENTS							
EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AL						Yes No
	AM						Yes No
	AN						Yes No
	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
KC	AR	16	Scheuner, D., et al., "Secreted amyloid β -protein similar to that in the senile plaques of Alzheimer's disease is increased <i>in vivo</i> by the presenilin 1 and 2 and APP mutations linked to familial Alzheimer's disease," <i>Nature Medicine</i> 2:864-870 (August 1996)
KC	AS	16	Sherrington, R., et al., "Cloning of a gene bearing missense mutations in early-onset familial Alzheimer's disease," <i>Nature</i> 375:754-760 (1995)
KC	AT	16	Sutcliffe, J.G., et al., "Antibodies That React with Predetermined Sites on Proteins," <i>Science</i> 219:660-666 (1983)

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FORM PTO-1449
INFORMATION DISCLOSURE STATEMENT

ATTY. DOCKET NO.
0609.4270001

APPLICATION NO.
09/065,902

APPLICANT
TANZI and KIM

JUL 29 1998

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April 24, 1998

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	AL						Yes No
	AM						Yes No
	AN						Yes No
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KC	AR	17	Tanzi, R.E., et al., "The Gene Defects Responsible for Familial Alzheimer's Disease," <i>Neurobiology of Disease</i> 3:159-168 (November 1996)
KC	AS	17	Thinakaran, G., et al., "Endoproteolysis of Presenilin 1 and Accumulation of Processed Derivatives In Vivo," <i>Neuron</i> 17:181-190 (July 1996)
KC	AT	17	Thompson, C.B., "Apoptosis in the Pathogenesis and Treatment of Disease," <i>Science</i> 267:1456-1462 (1995)

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	APPLICANT TANZI and KIM		
	FILING DATE April 24, 1998	GROUP 1643	GROUP 1800

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	AN					Yes No
	AO					Yes No
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KC	AR	18	Tomita, T., <i>et al.</i> , "The presenilin 2 mutation (N141I) linked to familial Alzheimer disease (Volga German families) increases the secretion of amyloid β protein ending at the 42nd (or 43rd) residue," <i>Proc. Natl. Acad. Sci. USA</i> 94:2025-2030 (March 1997)
KC	AS	18	Walter, J., <i>et al.</i> , "The Alzheimer's Disease-Associated Presenilins Are Differentially Phosphorylated Proteins Located Predominantly within the Endoplasmic Reticulum," <i>Molecular Medicine</i> 2:673-691 (November 1996)
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<i>KC</i>	AR	<u>19</u>	Wang, X., et al., "Cleavage of sterol regulatory element binding proteins (SREBPs) by CPP32 during apoptosis," <i>EMBO J.</i> 15:1012-1020 (March 1996)
<i>KC</i>	AS	<u>19</u>	Ward, C.L., et al., "Degradation of CFTR by the Ubiquitin-Proteasome Pathway," <i>Cell</i> 83:121-127 (1995)
<i>KC</i>	AT	<u>19</u>	Wasco, W., and Tanzi, R.E., "Molecular genetics of amyloid and apolipoprotein E in Alzheimer's disease," in <i>Neurobiology of Alzheimer's Disease</i> , Dawbarn, D., and Allen, S.J., eds., Bios Scientific Publishers Limited, Oxford, UK, pp. 51-76 (1995)
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FORM PTO-1449 INFORMATION DISCLOSURE STATEMENT				ATTY. DOCKET NO. 0609.4270001		APPLICATION NO. 09/065,902		JUL 29 1998 GROUP 1201
FILING DATE April 24, 1998				APPLICANT TANZI and KIM				
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KC	AR	20	Wiertz, E.J.H.J., <i>et al.</i> , "Sec61-mediated transfer of a membrane protein from the endoplasmic reticulum to the proteasome for destruction," <i>Nature</i> 384:432-438 (December 1996)					
KC	AS	20	Wolozin, B., <i>et al.</i> , "Participation of Presenilin 2 in Apoptosis: Enhanced Basal Activity Conferred by an Alzheimer Mutation," <i>Science</i> 274:1710-1713 (December 1996)					
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	APPLICANT TANZI and KIM	
	FILING DATE April 24, 1998	GROUP 1643 1644

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KC	AR	21	Yankner, B.A., et al., "Neurotrophic and Neurotoxic Effects of Amyloid β Protein: Reversal by Tachykinin Neuropeptides," <i>Science</i> 250:279-282 (1990)
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EXAMINER

Haven Clemens

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3/20/00

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